

APPLN. FILING DATE: JANUARY 26, 2004
TITLE: GOMPOSITION FOR AND TREATMENT OF
DEMYELINATING DISEASES AND PARALYSIS BY
ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539

SHEET 2 OF 25

SHEET 2 OF 25

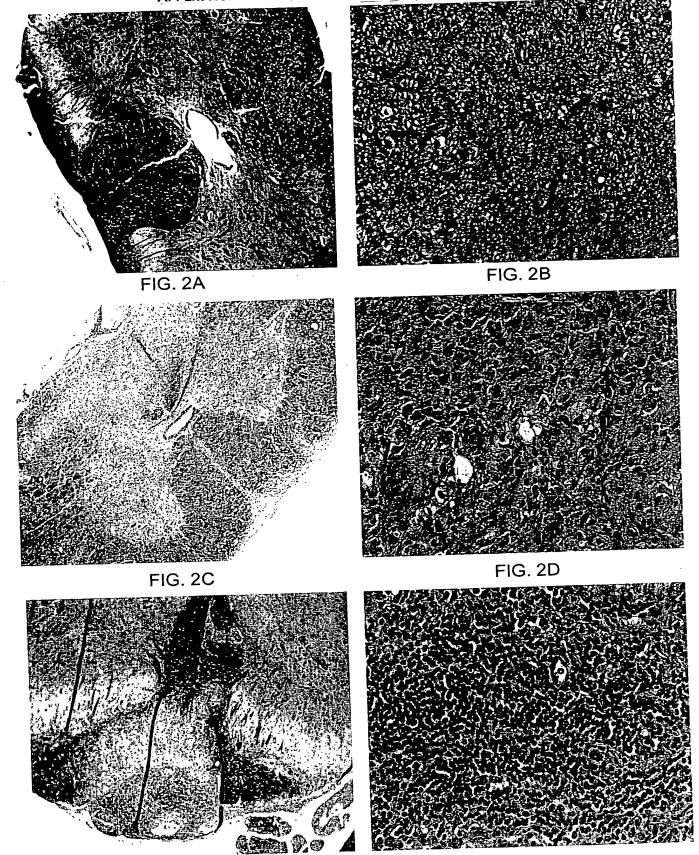


FIG. 2E

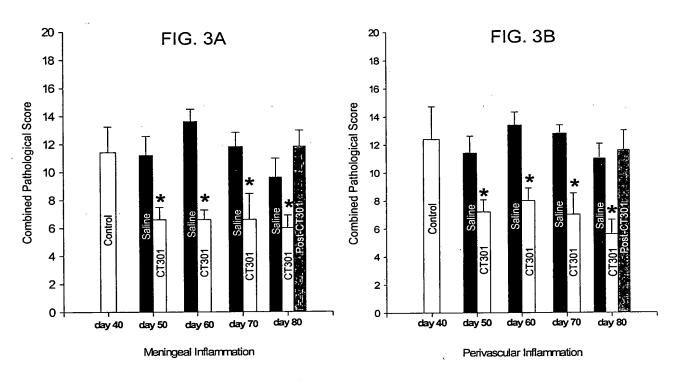
FIG. 2F

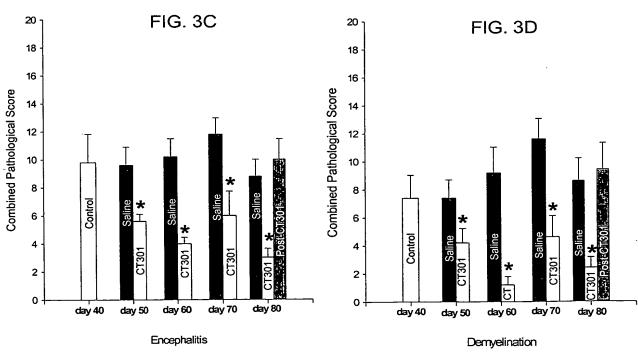
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APPLN. NO.: 10/763,539
SHEET 3 OF 25 **SHEET 3 OF 25** FIG. 2H FIG. 2G FIG. 2J FIG. 21

FIG. 2K FIG. 2L

APPLN. FILING DATE: JANUARY 26, 2004
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APPLN. No.: 10/763,539
SHEET 4 OF 25

SHEET 4 OF 25





APPLN. FILING DATE: JANUARY 26, 2004
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APPLN. No.: 10/763,539
SHEET 5 OF 25

SHEET 5 OF 25

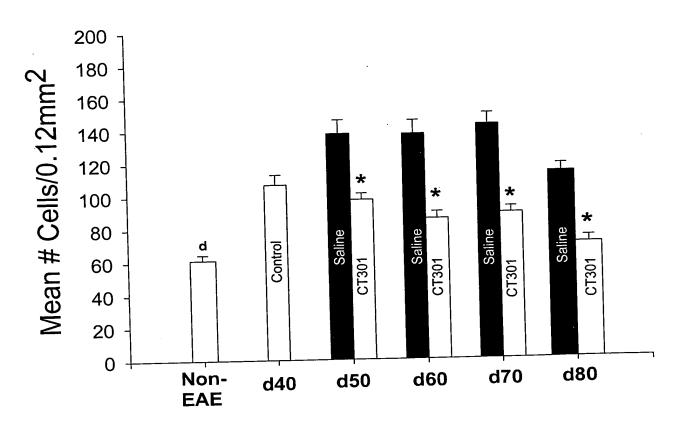
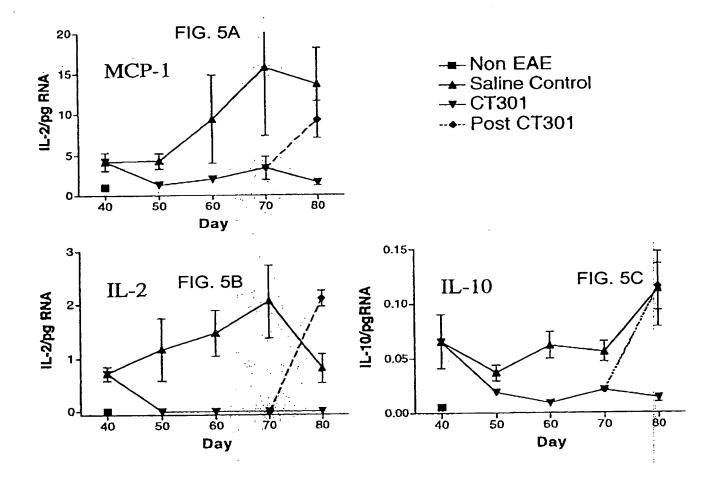


FIG. 4

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APPLN. NO.: 10/763,539
SHEET 6 OF 25 **SHEET 6 OF 25**



APPLN. FILING DATE: JANUARY 26, 2004
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DEMYELINATING DISEASES AND PARALYSIS BY
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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 7 OF 25



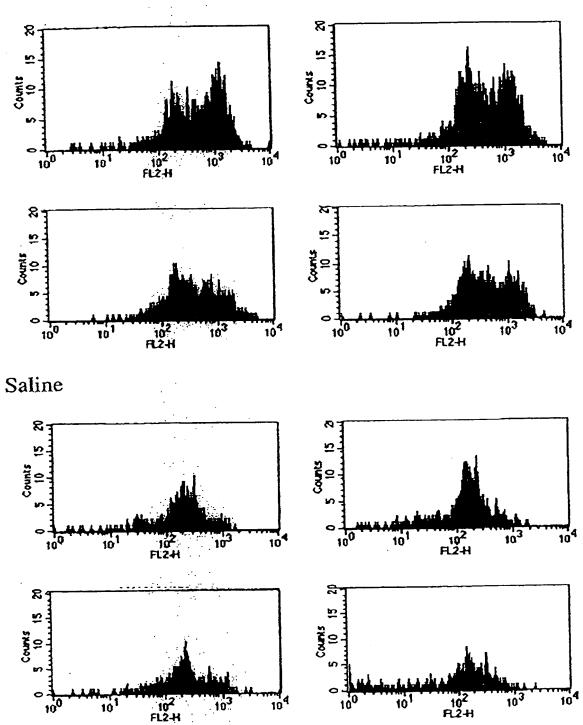


FIG. 6

APPLN. FILING DATE: JANUARY 26, 2004
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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 8 OF 25

Percentage α4 Integrin-High Blood Lymphocytes

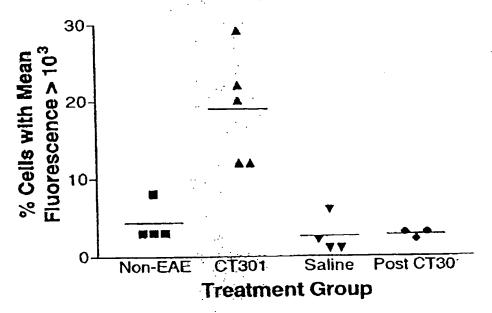


FIG. 7A

Expression of $\alpha 4$ Integrin on Blood Monocytes

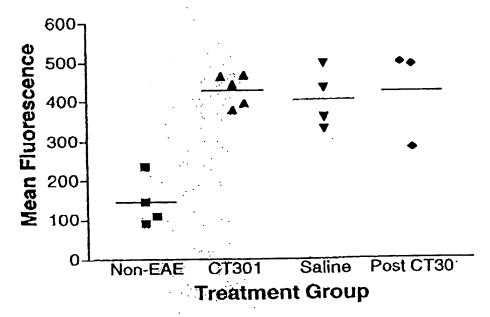


FIG. 7B

- Non-EAE
- ▲ CT301
- ▼ Saline
- Post CT301

Non-EAE

Post CT301

CT301

Saline

APPLN. FILING DATE: JANUARY 26, 2004
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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 9 OF 25 **SHEET 9 OF 25**

FIG. 8

APPLN. FILING DATE: JANUARY 26, 2004
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INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539 SHEET 10 OF 25

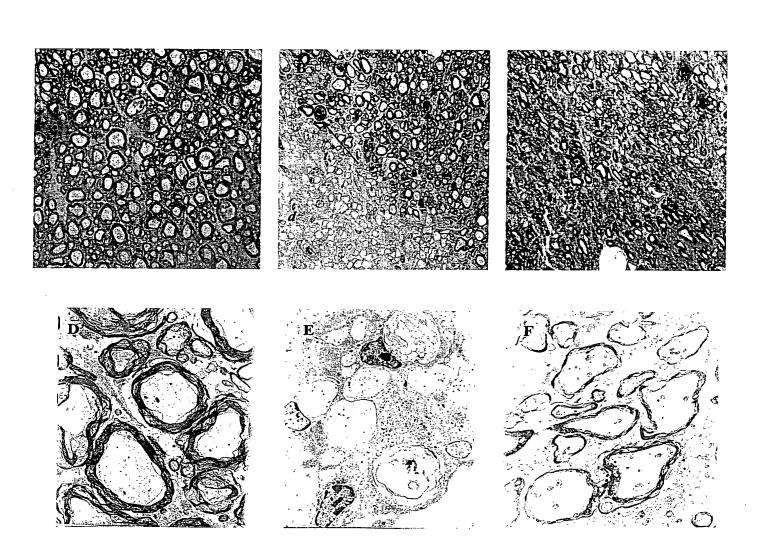
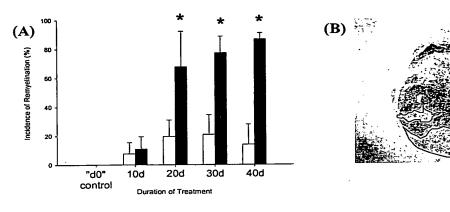
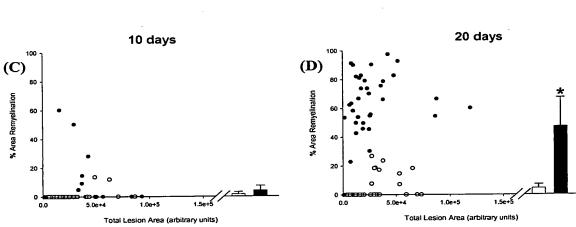


FIG. 9

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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 11 OF 2

SHEET 11 OF 25





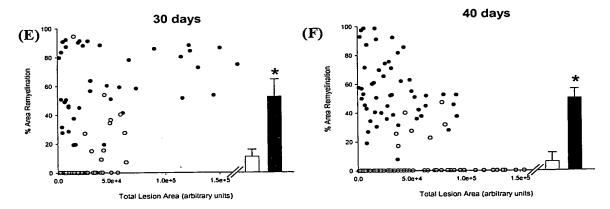


FIG. 10

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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 12 OF 25

agaaatgagaccgtctattcagttcctggggctcttgttgttctggcttcatgg
49 ----tctttactctggcagataagtcaaggaccccgagaacaacaagaccgaagtacc

[M R P S I Q F L G L L F W L H G LEADER

tgctcagtgtgacatccagatgacacagtctccatcctcactgtctgcatctct
103 -----acgagtcacactgtaggtctactgtgtcagaggtaggagtgacagacgtagaga

A Q C][D I Q M T Q S P S S L S A S L gggaggcaaagtcaccatcacttgcaagacaagccaagacattaacaagtatat ccctccgtttcagtggtagtgaacgttctgttcggttctgttaattgttcatata

G G K V T I T C][K T S Q D I N K Y M

A] [W Y Q H K P G K R P R L L I H] [Y T FR2

atctgcattacagccaggcatcccatcaaggttcagtggaagtgggtctgggag
265 ----tagacgtaatgtcggtccgtagggtagttccaagtcaccttcacccagaccctc

S A L Q P][G I P S R F S G S G S G R CDR2

FIG. 11 A

APPLN. FILING DATE: JANUARY 26, 2004
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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539

SHEET 13 OF 2 **SHEET 13 OF 25**

tcc 481 --agg

agattattccttcaacatcagcaacctggagcctgaagatattgcaacttatta 319 --tctaataaggaagttgtagtcgttggacctcggacttctataacgttgaataat DIA Ε Б S FR3 ttgtctacagtatgataatctgtggacgttcggtggaggcaccaagctggaaat 373 -aacagatgtcatactattagacacctgcaagccacctccgtggttcgaccttta W T][F G G G T K Y D N C][L Q FR4 CDR3 caaacgggctgatgctgcaccaactgtatccatcttcccaccatccacccggga gtttgcccgactacgacgtggttgacataggtagaagggtggtaggtggccct K] AGG-5'

FIG. 11B

		•																
		1		gaa	atg	cag	ctg	ggt	cat	gtt 	ctt	cct	gat	ggc	agt	ggt	tac	aggg
		-		ctt	tac	gtc	gac	cca	gta	caa	gaa	.gga	cta	.ccg	rca	cca	atg	tccc
	•		(M	K	С	s	W	V	М	F L	F EAD	L ER	М	A	V	v .	T	G
49	gt 	caa 	ttc	aga 	ggt:	tca 	gct	gca	gca 	gtc	rgg	ggc	aga	gct	tgt	gaa	gcc	aggg
	ca	gtt	aag	tct	cca	agt	cga	cgt	cgt	cag	acc	ccg	tct	cga	aca	ctt	cgg	tccc
	v	N	S]	(E	٧	Q ·	L	Q	Q	s	G	A	E	L	V F	K Rl	P	G
103	gc:	ctc	agt 	caa 	gtt:	gtc	ctg	cac	agc	ttc	tgg 	ctt	caa 	cat	taa 	aga 	cac	ctat
. •	cggagtcagttcaacaggacgtgtcgaagaccgaagttgtaatttctgtggata																	
	A	S	. V	K	L	S	С	Ť	A	S	Ģ	Ę	N	I	K)	[D	T	Y DR1
157	atacactgtgtgaagcagaggcctgaacagggcctggagtggattggaaggatt																	
	tatgtgacacacttcgtctccggacttgtcccggacctcacctaaccttcctaa																	
	I	H]	(C	V	К	Q	R	P	E	Q FI	G R2	L	E	W	I	G]	[R	I
211	gatcctgcgaatggttatactaaatatgacccgaagttccagggcaaggccact																	
	cta	agg	acg	ctt:	acca	aata	atg	att:	tata	act	333	ctt	caa	ggt	ccc	gtt	ccg	gtga
	D	P	A	N	G	Y CDI	T R2	K	Y	D	P	K	F	Q	G]	(K	A	T
265	ataacagctgacacatcctccaacacagcctacctgcagctcagcagcctgaca																	
	tat	tg.	tcga	acto	gtgt	ago	gag	gtt	gtgi	tcg	gat	gga	cgt	cga	gtc	gtc	gga	ctgt
	I	T	A	D	T	s	S	N	T	A	Y	L	Q	L	S FR3	s	L	T

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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 14 OF 2

SHEET 14 OF 25

FIG. 12A

APPLN. FILING DATE: JANUARY 26, 2004
TITLE: COMPOSITION FOR AND TREATMENT OF
DEMYELINATING DISEASES AND PARALYSIS BY
ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 15 OF 25

cggttttgctgtgggggtagacagataggtgaccgggccctagg

s s]

427

APPLN. FILING DATE: JANUARY 26, 2004
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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 16 OF 25

•			
FR1	CDR1	FR2	CDR2
1 2	3	4	5
12345678901234567890123	45678901234 ******	567890123456789	0123456
DIQMTQSPSSLSASLGGKVTITC	KTSQDINKYMA	WYQHKPGKRPRLLIH	YTSALQP
DIQMTQSPSSLSASVGDRVTITC	QASQDIIKYLN	WYQQTPGKAPKLLIY	EASNLQA
DIQMTQSPSSLSASVGDRVTITC	KTSQDINKYMA	WYQQTPGKAPRLLIH	YTSALQP
		R	
	1 2 12345678901234567890123 * DIQMTQSPSSLSASLGGKVTITC DIQMTQSPSSLSASVGDRVTITC DIQMTQSPSSLSASVGDRVTITC	1 2 3 12345678901234567890123 45678901234 * ********* DIQMTQSPSSLSASLGGKVTITC KTSQDINKYMA DIQMTQSPSSLSASVGDRVTITC QASQDIIKYLN DIQMTQSPSSLSASVGDRVTITC KTSQDINKYMA	1 2 3 4 12345678901234567890123 45678901234 567890123456789

APPLN. FILING DATE: JANUARY 26, 2004
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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 17 OF 25

		FR1		CDR1	FR2	C	DR2	
	1	. 2	3		4	5	6	
	12345678901	23456789012	34567890	12345	6789012345		45678901234 **	5
21.6	EVQLQQSGAEL	VKPGASVKLSC	rasgfnik	DTYIH	CVKQRPEQGL	EWIG RIDPA	NGYTKYDPKFQ	}Ġ
2*CL	QVQLVQSGAEV	KKPGASVKVSCI	KASGYTFT	SYAMH	WVRQAPGQRL	EWMG WINAG	NGNTKYSQKFÇ	ĮG
На	QVQLVQSGAEV	KKPGASVKVSC	KASG <u>FNIK</u>	DTYIH	WVRQAPGQRL	EWMB RIDPA	NGYTKYDPKFÇ	ĮG
НЬ			FNIK	·	G-		·	
НС			FNIK					
		÷	-					
		FR3			CDR3	FR4		
	. 7	8	9	-	10	11		
	67890123456	5789012ABC34	567890123	34 5678 *	390ABCDEF12	345678901	.23	
21.6	KATITADTSSN	TAYLQLSSLTS	edtavyfc <i>i</i>	AR EGY	YGNYGVYAMDY	WGQGTSVTV	'SS	
2*CL	RVTITRDTSAS	STAYMELSSLRS	EDTAVYYC	AR GGY	YGSGSNY	WGQGTLVTV	'SS	
Ha _	RVTIT <u>A</u> DTSAS	TAYMELSSLRS	EDTAVYYC	AR EGY	YGNYGVYAMDY	WGQGTLVTV	'SS	
НЬ	A							
НС	A			<u>F</u>			· 	

ADMINISTRATION OF REMYELINATING AGENTS INVENTOR(S): STEVE J. KARLIK ET AL.

APPLN. No.: 10/763,539

SHEET 18 OF 2 **SHEET 18 OF 25** HindIII KOZAK SEOUENCE aagett<u>gccgccaccatg</u>agaccgtctattcagttcctgggggctcttgttgttc ttcgaacggcggtggtactctggcagataagtcaaggaccccgagaacaacaag (M R P LEADER tggcttcatggtgctcagtgtgacatccagatgacacagtctccatcctcactg accgaagtaccacgagtcacactgtaggtctactgtgtcagaggtaggagtgac G A Q C][D I Q M FR1 tctgcatctGTAggaGATAGAgtcaccatcacttgcaagacaagccaagacatt agacgtagaCATcctCTATCTcagtggtagtgaacgttctgttcggttctgtaa ASVGDRV T I T C] [K T S CDR1 aacaagtatatggcttggtaccaaCAGACAcctggaaaaGCTcctaggctgctc 163 -ttgttcatataccgaaccatggttGTCTGTggaccttttCGAggatccgacgag M A W Y Q QP G K atacattacacatctgcattacagccaggcatcccatcaaggttcagtggaagt tatgtaatgtgtagacgtaatgtcggtccgtagggtagttccaagtcaccttca I - H] [Y Q P][G I S gggtctgggagagattatACTttcACCatcagcAGCctgCAGcctgaagatatt cccagaccctctctaataTGAaagTGGtagtcgTCGgacGTCggacttctataa T T S S. L Q P E

APPLN. FILING DATE: JANUARY 26, 2004 TITLE: COMPOSITION FOR AND TREATMENT OF DEMYELINATING DISEASES AND PARALYSIS BY

FIG. 15A

FR3

APPLN. FILING DATE: JANUARY 26, 2004
TITLE: COMPOSITION FOR AND TREATMENT OF
DEMYELINATING DISEASES AND PARALYSIS BY
ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 19 OF 25

K V E I K]

APPLN. FILING DATE: JANUARY 26, 2004
TITLE: COMPOSITION FOR AND TREATMENT OF
DEMYELINATING DISEASES AND PARALYSIS BY
ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 20 OF 25

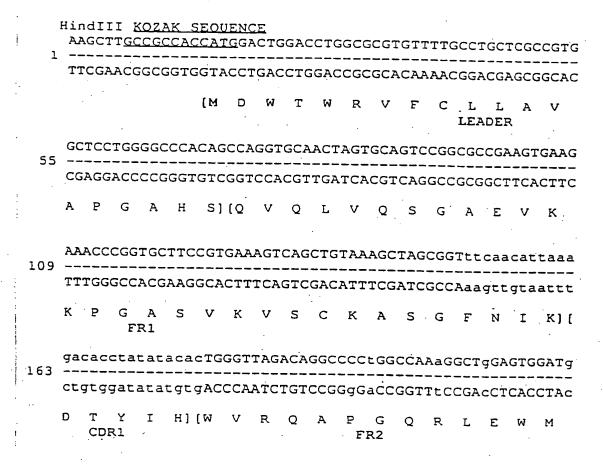


FIG. 16A

APPLN. FILING DATE: JANUARY 26, 2004
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DEMYELINATING DISEASES AND PARALYSIS BY
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INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
SHEET 21 OF 25

GGaaggattgatcctgcgaatggttatactaaatatgacccgaagttccagggc 217 CCttcctaactaggacgcttaccaatatgatttatactgggcttcaaggtcccg K Y Y T .D K G][R I D G CDR2 cgggtcACCatcACCgcaGACACCTCTgccagcACCGCCTACATGGAACTGTCC 271 gcccagTGGtagTGGcgtCTGTGGAGAcggtcgTGGCGGATGTACCTTGACAGG RVTITAD T s A S Т FR3 AGCCTGCGCTCCGAGGACACTGCAGTCTACTACTGCGCCagagagggatattat 325 ---TCGGACGCGAGGCTCCTGTGACGTCAGATGATGACGCGGEctctcccctataata SLRSEDTAVY $\verb"ggtaactacggggtctatgctatgGACTAcTGGGGtCAaGGaACCCTTGTCACC"$ 379 ccattgatgccccagatacgatacCTGATgACCCCaGTtCCtTGGGAACAGTGG G N Y G V Y A M D Y][W G QGT CDR3 FR4 SPLICE DONOR SITE BamHI GTCtccTCAGGTGAGTGGATCC CAGaggAGTCCACTCACCTAGG V S S]

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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 22 OF 25

- (A) LENGTH: 109 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- N Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gly Ser Pro Lys Leu Leu Ile Tyr Tyr Ala Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys C

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ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539 SHEET 23 OF 25

- (A) LENGTH: 114 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- N Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ser Leu Val Xaa Xaa Ser Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Leu Pro Glu Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys C

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INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. No.: 10/763,539
SHEET 24 OF 25

- (A) LENGTH: 125 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- N Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Lys Phe Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Tyr Tyr Tyr Asp Ser Xaa Val Gly Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Xaa Val Thr Val Ser Ser C

APPLN. FILING DATE: JANUARY 26, 2004
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INVENTOR(s): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539 SHEET 25 OF 25

- (A) LENGTH: 129 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

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N - Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

Gly Trp Ile Asn Pro Tyr Gly Asn Gly Asp Thr Asn Tyr Ala Gln Lys

Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr

Cys Ala Arg Ala Pro Gly Tyr Gly Ser Gly Gly Gly Cys Tyr Arg Gly Asp

Tyr Xaa Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser - C
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